Kaohsiung Journal of Medical Sciences (2015) 31, 150–155

Available online at www.sciencedirect.com

ScienceDirect

journal homepage: http://www.kjms-online.com

ORIGINAL ARTICLE

A comparison of propofol target controlled infusion-based and sevoflurane-based anesthesia in adults undergoing elective anterior cervical discectomy and fusion

Ching-Kuo Lin [a,b], Yu-Tung Feng [c], Shiuh-Lin Hwang [b,d], Chih-Lung Lin [b,d], King-Teh Lee [b,d], Kuang-I Cheng [b,e,*]

[a] *Department of Emergency Medicine, Kaohsiung Municipal Ta-Tung Hospital, Kaohsiung, Taiwan*
[b] *Faculty of Medicine, School of Medicine, Kaohsiung Medical University, Kaohsiung, Taiwan*
[c] *Department of Healthcare Administration and Medical Informatics, Kaohsiung Medical University, Kaohsiung, Taiwan*
[d] *Department of Surgery, Kaohsiung Medical University Hospital, Kaohsiung, Taiwan*
[e] *Department of Anesthesiology, Kaohsiung Medical University Hospital, Kaohsiung, Taiwan*

Received 13 March 2014; accepted 22 September 2014
Available online 20 January 2015

KEYWORDS
Anterior cervical discectomy and fusion;
Inhalational sevoflurane;
Propofol TCI;
Quality anesthesia

Abstract The target controlled infusion (TCI) of propofol with fentanyl facilitates easy titration of the depth of anesthesia, and thereby may improve the quality of anesthesia. The aim of this study is to investigate if propofol TCI-based anesthesia is practical for anterior cervical discectomy and fusion (ACDF), one of the most common surgical interventions in spine procedures, when compared with sevoflurane-based anesthesia with respect to the quality of anesthesia. Patients were classified into two groups according to the anesthesia regimen of maintenance of anesthesia with fentanyl and either propofol TCI (group FP) or inhalational sevoflurane (group FS), respectively. The primary endpoint was to evaluate quality of anesthesia and extubation time. Secondary endpoints were hemodynamic stability during the operation, operative fentanyl consumption, and postoperative complications. The study results revealed there were comparable results on time to extubation, changes in intraoperative hemodynamic parameters, and the occurrence of postoperative complications between the groups. No differences in average length of intensive care unit (ICU) stay and hospital stay were noticed. However, opioid consumption and blood loss during the operation for patients in group FP were significantly higher than those of patients in group FS (551.28 ± 193.98 vs. 446.86 ± 177.15 μg, $p = 0.005$; 52.06 ± 58.25 vs. 28.33 ± 40.74 mL, $p = 0.019$, respectively). In these adult

Conflicts of interest: All authors declare no conflicts of interest.

* Corresponding author. Number 100, Tzyou First Road, San-Ming District 80708, Kaohsiung, Taiwan.
E-mail address: kuaich@kmu.edu.tw (K.-I. Cheng).

http://dx.doi.org/10.1016/j.kjms.2014.12.002

patients undergoing ACDF, propofol TCI-based anesthesia appears to be as efficacious as sevoflurane-based anesthesia but consumed more fentanyl and experienced higher blood loss.

Introduction

Anterior discectomy with or without fusion is the most common surgical intervention performed by spine surgeons for degenerative cervical spondylosis. When surgery is indicated, the choice of operative approaches including anterior, posterior, and combined procedures becomes a significant part in the optimal management of the disease [1]. Anterior cervical discectomy and fusion (ACDF) procedures then become one of the most common procedures performed in spinal surgery [2].

Including three components such as muscle relaxation, unconsciousness, and analgesia, general anesthesia introduces lack of response and recall to noxious stimuli [3]. As well as obtaining a rapid and safe level of depth of anesthesia during the induction phase, the anesthesiologist is also concerned with providing a comfortable and precise return to consciousness after surgery [4]. The type of surgery and patient variability are key factors for an anesthesiologist to consider when choosing anesthetic agents and/or changing drug dosage during the maintenance of anesthesia [5].

Because of its low blood-gas partition coefficient, sevoflurane is able to facilitate rapid emergence from anesthesia and is thus used in a wide range of clinical practices [6,7]. However, emergence agitation and excitatory behavior are frequently seen when sevoflurane is offered to pediatric patients [7—9]. Whether this might entail risks of unexpected events for the adult patients receiving cervical spine surgery and further disturb subsequent postoperative neurological examinations remains unknown. Besides, several studies suggest that postoperative agitation and restlessness are mainly caused by pain, i.e., inadequate pain relief during the emergence period, and that the concomitant use of an opioid provides smoother anesthetic management [6,10,11].

The target controlled infusion (TCI) system was recently introduced in clinical practices in Taiwan. Total intravenous anesthesia (TIVA) with fentanyl combined with TCI of propofol facilitates easy titration of depth of anesthesia and has therefore become an attractive alternative anesthesia regimen, which might improve the quality of emergence from anesthesia in Western patients [6,12]. Interindividual variability in pain perception is believed to exist because of genetic polymorphism [13]. Whether TIVA with TCI is well adopted in the southern Taiwanese population is of interest.

The present study was designed to investigate if propofol TCI-based anesthesia was practical for ACDF when compared with sevoflurane-based anesthesia with respect to the quality of anesthesia in a medical center in southern Taiwan.

Methods

All adult patients aged 23—75 years who underwent ACDF in the Neuroscience Center at Kaohsiung Medical University Hospital from January 2009 to December 2011 were enrolled in the study and data were collected and then reviewed retrospectively. The Institutional Review Board approved the study (KMUH-IRB-990271). Patients were excluded based on C1—2 involvement, trauma, neoplasia, or previous cervical fusion and then further classified into two groups according to the anesthesia regimen they received: (i) maintenance of anesthesia with fentanyl (Glaxosmithkline Manufacturing S.P.A., Verrona, Italy) and propofol (B.Braun Melsungen AG, Melsungen, Germany) TCI (group FP); and (ii) maintenance of anesthesia with fentanyl and inhalational sevoflurane (group FS). A dedicated anesthesia team for neurosurgery decided on the procedure for maintenance of anesthesia on the operation day.

Information regarding age, sex, medical comorbidities, history of preoperative medicine, history of smoking, body mass index (BMI), and surgical details were collected, and routine blood workup, including blood cell count, prothrombin and partial thromboplastin times, and international normalized ratio, were routinely obtained. International Classification of Diseases-9 (ICD-9) diagnosis codes were used to generate a Charlson comorbidity index (graded 0 or $\geq$ 1; categorical variables) for each patient. For patients assigned to group FP, patients were induced with propofol 5 μg/mL (effect site of concentration, Ce value) using a TCI pump (EP-1809-1; Fresenius Kabi, Bad Homburg, Germany) and fentanyl 2 μg/kg. The Ce value was continuously monitored during induction, intubation, and operation for adequate maintenance of anesthesia depth. To facilitate intubation, rocuronium 0.6 mg/kg was offered. After successful intubation, propofol TCI was titrated to 1.5—5.0 μg/mL according to the level of unconsciousness, and fentanyl 1—3 μg/kg infusion was maintained with intermittent fentanyl 50 μg boluses offered according to changes in heart rate or blood pressure over 20% from baseline by surgical stimuli. In addition, rocuronium 0.3 mg/kg/h were continuously offered. Patients assigned to group FS were induced with fentanyl 2 μg/kg and thiamylal 5 mg/kg, and rocuronium 0.6 mg/kg was also offered to facilitate intubation. Following successful intubation, fentanyl 1—3 μg/kg infusion was maintained with intermittent fentanyl 50 μg boluses offered according to changes in heart rate or blood pressure over 20% from baseline by surgical stimuli. In addition, rocuronium 0.3 mg/kg/h were continuously offered. Anesthesia was maintained with inhaled sevoflurane (Ultane; Abbott Laboratories, Chicago, IL, USA) at 1.5—2.0 minimum alveolar concentration (MAC) end-tidal.

Standard cardiovascular and respiratory monitoring included continuous electrocardiography (ECG), pulse

oximetry, end-tidal CO_2, and intermittent (2.5-minute interval) noninvasive blood pressure measurement. The anesthetic depth was titrated mainly with blood pressure and heart rate according to the anesthesia protocol. Immediately after the completion of surgery, i.e., completion of dressing of the surgical field, all agents for balanced anesthesia were discontinued and patients were then transferred to the intensive care unit (ICU) for further observation and care. Ventilation was assisted until the recovery of spontaneous breathing, and patients were then extubated when all seven of the following criteria were met: (1) regular breathing without retraction; (2) respiratory rate $>$ 8 breaths/min and end-tidal CO_2 $<$ 45 mmHg; (3) oxygen saturation (SaO_2) $>$ 95% with fraction of inspired oxygen (FiO_2) of 100%; (4) swallowing reflex present on clinical assessment; (5) esophageal temperature between 36°C and 37°C; (6) hemodynamic stability ($\leq$ 15 mmHg change in blood pressure from baseline); and (7) patient cooperative, oriented, able to respond to commands. The time to extubation, defined as the duration between the completion of dressing of the surgical field and tracheal extubation, was recorded. Postoperative nausea and vomiting (PONV) was treated with metoclopramide as needed. The primary endpoint was the time to extubation. Secondary endpoints were hemodynamic stability, operative fentanyl consumption, and postoperative complications.

Statistical analyses for the study were performed using SPSS 12.0 for Windows (SPSS Inc., Chicago, IL, USA). Demographic and clinical data were analyzed using the Student *t* test or Pearson χ^2 test as appropriate. Kaplan–Meier curves for complications were constructed, and a log-rank test was used to compare the differences between groups. Data for patients who experienced complications during ICU stay after surgical procedure were censored. Two-sided tests were used for all analyses. A *p* value of less than 0.05 was considered statistically significant.

Results

During a period of 36 months, 114 patients who suffered from degenerative cervical spondylosis and underwent ACDF were included in the study. Among them, 13 patients met various exclusion criteria and therefore were excluded, two because of C1–2 involvement, six for trauma, one for neoplasia, and four for previous cervical fusion. As a result, 101 patients were evaluated (50 in the propofol TCI group and 51 in the inhalational sevoflurane group). No significant differences in any demographic characteristics between groups were found (Table 1).

The preliminary results of analyses of the study were shown in Table 2, which demonstrated that no differences of anesthesia time, operation time, time to extubation, intubation period, and the occurrence of postoperative complications were found. Change in mean blood pressure (both systolic and diastolic) and heart rate during anesthesia were similar in the two groups. No differences of both average length of ICU stay and hospital stay were noticed. However, opioid consumption and blood loss during operation for patients in group FP were significantly higher than those of patients in group FS (551.28 $\pm$ 193.98 vs. 446.86 $\pm$ 177.15 μg, $p = 0.005$; 52.06 $\pm$ 58.25 vs. 28.33 $\pm$ 40.74 mL, $p = 0.019$, respectively).

Rates of episodes of acute complications that included mild sore throat, PONV, and mild dizziness were similar between groups (group FP 34.0% vs. group FS 47.1%,

Table 1 Patient demographic and baseline characteristics.

	Group FP ($n = 50$)	Group FS ($n = 51$)	*p*
Age (y)	52.44 $\pm$ 14.70	51.65 $\pm$ 14.11	0.782
Sex (F/M), no.	26/24	27/24	0.938
BMI	23.77 $\pm$ 3.87	24.11 $\pm$ 3.70	0.653
CCI ($\geq$1), no. (%)	26 (52.0)	27 (52.9)	0.938
Systolic blood pressure (mmHg)			
Baseline	140.08 $\pm$ 21.51	136.32 $\pm$ 17.63	0.427
During anesthesia	132.38 $\pm$ 14.30	131.41 $\pm$ 20.32	0.814
Diastolic blood pressure (mmHg)			
Baseline	81.21 $\pm$ 11.94	80.45 $\pm$ 12.89	0.809
During anesthesia	74.29 $\pm$ 11.91	76.72 $\pm$ 13.90	0.464
Heart rate (beats/min)			
Baseline	70.38 $\pm$ 14.26	74.84 $\pm$ 13.34	0.190
During anesthesia	78.08 $\pm$ 13.27	84.44 $\pm$ 15.90	0.095
AST (U/L)	23.42 $\pm$ 8.28	30.51 $\pm$ 25.94	0.196
ALT (U/L)	24.42 $\pm$ 17.73	29.27 $\pm$ 23.64	0.374
Serum creatinine (g/dL)	0.86 $\pm$ 0.31	0.94 $\pm$ 0.90	0.687
ASA physical status, no. (%)			
Class 2	39 (78.0)	40 (78.4)	0.942
Class 3	11 (22.0)	11 (21.6)	

Values are mean $\pm$ SD, unless otherwise specified.
ALT = alanine transaminase; ASA = American Society of Anesthesiologists; AST = aspartate aminotransferase; FP = maintenance of anesthesia with fentanyl and propofol TCI; FS = maintenance of anesthesia with fentanyl and inhalational sevoflurane; SD = standard deviation; TCI = target controlled infusion.

Table 2 Clinical outcomes and medical resource usage.

	Group FP (n = 50)	Group FS (n = 51)	p
Anesthesia time (h)	3.65 ± 1.14	3.49 ± 0.82	0.395
Operation time (h)	2.74 ± 1.06	2.61 ± 0.79	0.493
Time to extubation (h)	2.59 ± 1.35	2.50 ± 1.14	0.712
Intubation duration (h)	6.28 ± 1.59	6.07 ± 1.21	0.448
Change in			
SBP (mmHg)	12.37 ± 9.78	11.57 ± 9.80	0.679
DBP (mmHg)	16.29 ± 11.63	16.92 ± 12.09	0.790
HR	11.58 ± 11.16	11.84 ± 11.06	0.908
Opioid consumption (μg)	551.28 ± 193.98	446.86 ± 177.15	0.005*
Complications, no. of patients (%)	17 (34.0)	24 (47.1)	0.225
PONV, no.	7 (14.0)	11 (21.6)	0.437
Mild sore throat, no.	8	9	
Mild dizziness, no.	2	4	
Blood loss (mL)	52.06 ± 58.25	28.33 ± 40.74	0.019*
Length of ICU stay (d)	1.24 ± 0.47	1.20 ± 0.57	0.705
Length of hospital stay (d)	8.55 ± 5.47	8.08 ± 2.79	0.585

Values are mean ± SD, unless otherwise specified.
*$p < 0.05$.
DBP = diastolic blood pressure; FP = maintenance of anesthesia with fentanyl and propofol TCI; FS = maintenance of anesthesia with fentanyl and inhalational sevoflurane; HR = heart rate; ICU = intensive care unit; PONV = postoperative nausea and vomiting; SBP = systolic blood pressure; SD = standard deviation; TCI = target controlled infusion.

p = 0.225). Kaplan–Meier analysis was further used to discover if the complication was related to time to extubation. No significant difference between the curves for acute complications in the two groups was found (Fig. 1; p = 0.146, log-rank test). There were no hematomas, airway complications, or deaths. No blood transfusions were needed.

Discussion

An ideal anesthetic regimen for cervical spine surgery would provide a smooth emergence without hazardous coughing or bucking in terms of neck stabilization and quick recovery time, which allows immediate neurologic assessment and early detection of potential postoperative

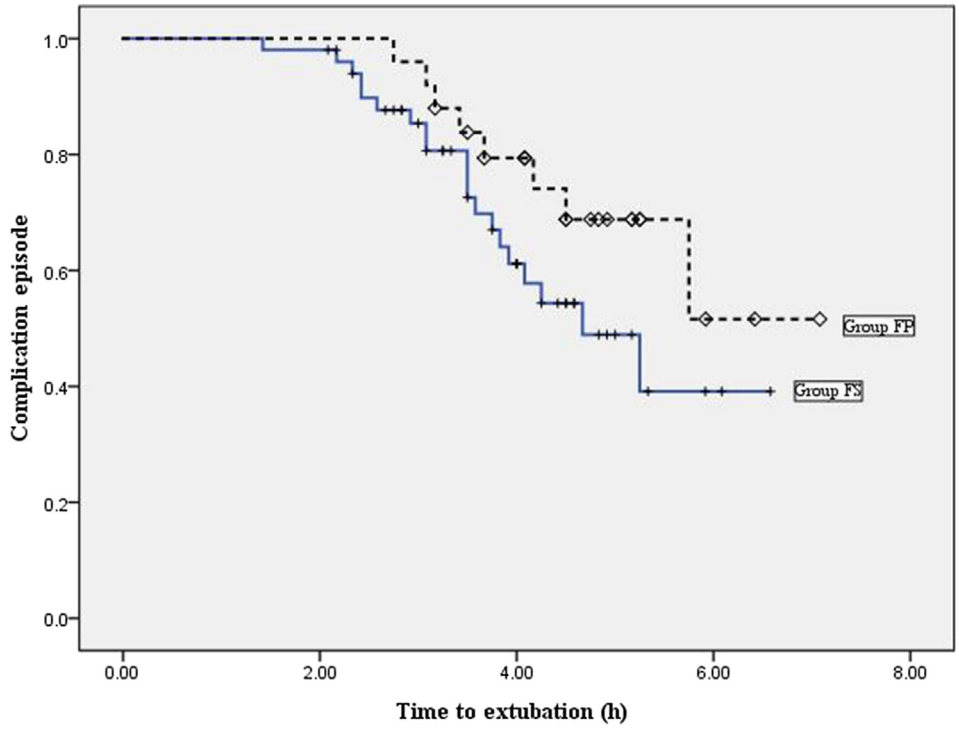

Figure 1. The occurrence of acute complications in the study groups. FP group = maintenance of anesthesia with fentanyl and propofol target controlled infusion (TCI); FS group = maintenance of anesthesia with fentanyl and inhalational sevoflurane.

complications to exclude surgical failure [6,13,14]. The study was designed with the focus on the emergence period from different anesthesia regimens; our aim was to describe the profile in ACDF that facilitates rapid neurological examination to exclude surgical failure or potentially dangerous hematoma formation. In patients receiving elective ACDF in this study, maintenance of anesthesia with fentanyl and propofol TCI according to a predetermined algorithm based on hemodynamic data was not associated with a later time to extubation compared with maintenance of anesthesia with fentanyl and inhalational sevoflurane. A difference in time to extubation would have clinical relevance only if it is associated with differences in patient outcomes or resource utilization [14]. However, later time to extubation was not associated with any endpoint of patient outcomes or resource utilization in our study.

Total opioid consumption during operation for patients with maintenance of anesthesia with fentanyl and propofol TCI were significantly higher. It is possible that the time to extubation might not be influenced by the amount of propofol offered or by fentanyl, although Djian et al [15] found that the time to extubation is influenced more by the amount of propofol administered than the opioid. It is also possible that more fentanyl has to be provided to ensure an adequate state of analgesia for operation in patients with maintenance of anesthesia with fentanyl and propofol TCI because mean systolic (diastolic) blood pressure and mean heart rate were similar in the groups at all times after blinded adjustment of the infusion rate of fentanyl based on hemodynamic parameters to keep appropriate anesthesia depth. In other words, maintenance of anesthesia with fentanyl and inhalational sevoflurane reduces opioid requirements.

Blood loss during the operation for patients with maintenance of anesthesia with fentanyl and propofol TCI was also significantly higher. However, the blood loss in the study groups was not associated with longer length of observational ICU stay or hospital stay. The causative relationship of blood loss and treatment outcomes was infrequently discussed in the previous studies [15]. No patient in the study required emergent reintervention during the ICU or hospital stay after surgery.

The incidence of complications was insignificantly different in the two study groups ($p = 0.225$). The incidence of PONV was insignificantly different in the two groups (14.0% vs. 21.6%, $p = 0.437$), in which the low incidence of PONV for patients with maintenance of anesthesia with fentanyl and propofol TCI was in accordance with previous reports [14]. Intraoperative opioid administration is believed to be a strong possible causative factor for PONV [7]. Patients with maintenance of anesthesia with fentanyl and propofol TCI in the study required significantly more fentanyl, however, the incidence of PONV in the group remained low. This might be related to the use of propofol, which is known to possess antiemetic properties [16,17]. Nevertheless, comments on adverse events were not consistent.

Our study had some limitations. First, data were retrospectively collected without a proper prospective randomized design. Second, anesthetic depth was titrated mainly with blood pressure and heart rate according to the anesthesia protocol; however, the bispectral index (BIS) is one of several technologies used most frequently to monitor depth of anesthesia. Third, data were collected from a single department (the Neuroscience Center). However, ACDF is performed in the Orthopedics Department as well. Bias might occur through a single-department retrospective study design and thus limit its generalizability. A large, prospective randomized study is warranted to determine factors impacting patient outcomes and resource utilization of patients receiving similar regimens of maintenance of anesthesia for ACDF.

In conclusion, in these adult patients undergoing ACDF, propofol TCI-based anesthesia appears to be as efficacious as sevoflurane-based anesthesia but consumed more fentanyl and experienced higher blood loss.

Acknowledgments

The authors thank Mr Richard H. Davis for his gratuitous assistance with the language editing of the manuscript. The authors also thank Yu-Ping Weng, R.N., anesthetist, for her assistance in the collection of data.

References

[1] Feng YT, Hwang SL, Lin CL, Lee IC, Lee KT. Safety and resource utilization of anterior cervical discectomy and fusion. Kaohsiung J Med Sci 2012;28:495—9.
[2] Sheperd CS, Young WF. Instrumented outpatient anterior cervical discectomy and fusion: is it safe? Int Surg 2012;97:86—9.
[3] Nunes CS, Ferreira DA, Antunes L, Amorim P. Clinical variables related to propofol effect-site concentrations at recovery of consciousness after neurosurgical procedures. J Neurosurg Anesthesiol 2005;17:110—4.
[4] Larsen B, Seitz A, Larsen R. Recovery of cognitive function after remifentanil-propofol anesthesia: a comparison with desflurane and sevoflurane anesthesia. Anesth Analg 2000;90:168—74.
[5] Nunes CS, Ferreira DA, Antunes L, Lobo F, Santos IA, Amorim P. Individual effect-site concentrations of propofol at return of consciousness are related to the concentrations at loss of consciousness and age in neurosurgical patients. J Clin Anesth 2009;21:3—8.
[6] Inoue Y, Koga K, Sata T, Shigematsu A. Effects of fentanyl on emergence characteristics from anesthesia in adult cervical spine surgery: a comparison of fentanyl-based and sevoflurane-based anesthesia. J Anesth 2005;19:12—6.
[7] Ko YP, Huang CJ, Hung YC, Su NY, Tsai PS, Chen CC, et al. Premedication with low-dose oral midazolam reduces the incidence and severity of emergence agitation in pediatric patients following sevoflurane anesthesia. Acta Anaesthesiol Sin 2001;39:169—77.
[8] Goa KL, Noble S, Spencer CM. Sevoflurane in paediatric anaesthesia: a review. Paediatr Drugs 1999;1:127—53.
[9] Beskow A, Westrin P. Sevoflurane causes more postoperative agitation in children than does halothane. Acta Anaesthesiol Scand 1999;43:536—41.
[10] Uezono S, Goto T, Terui K, Ichinose F, Ishguro Y, Nakata Y, et al. Emergence agitation after sevoflurane versus propofol in pediatric patients. Anesth Analg 2000;91:563—6.
[11] Cohen IT, Hannallah RS, Hummer KA. The incidence of emergence agitation associated with desflurane anesthesia in children is reduced by fentanyl. Anesth Analg 2001;93:88—91.

[12] Vuyk J, Mertens MJ, Olofsen E, Burm AG, Bovill JG. Propofol anesthesia and rational opioid selection: determination of optimal EC50-EC95 propofol-opioid concentrations that assure adequate anesthesia and a rapid return of consciousness. Anesthesiology 1997;87:1549—62.
[13] Cheng KI, Lin SR, Chang LL, Wang JY, Lai CS. Association of the functional A118G polymorphism of OPRM1 in diabetic patients with foot ulcer pain. J Diabetes Complications 2010;24:102—8.
[14] Palmer JD, Sparrow OC, Iannotti F. Postoperative hematoma: a 5-year survey and identification of avoidable risk factors. Neurosurgery 1994;35:1061—4. discussion 4—5.
[15] Djian MC, Blanchet B, Pesce F, Sermet A, Disdet M, Vazquez V, et al. Comparison of the time to extubation after use of remifentanil or sufentanil in combination with propofol as anesthesia in adults undergoing nonemergency intracranial surgery: a prospective, randomized, double-blind trial. Clin Ther 2006;28:560—8.
[16] Gao Y, Liu M, Li T, Huang F, Tang T, Xiang Z. A meta-analysis comparing the results of cervical disc arthroplasty with anterior cervical discectomy and fusion (ACDF) for the treatment of symptomatic cervical disc disease. J Bone Joint Surg Am 2013;95:555—61.
[17] Tramer M, Moore A, McQuay H. Propofol anaesthesia and postoperative nausea and vomiting: quantitative systematic review of randomized controlled studies. Br J Anaesth 1997; 78:247—55.